United States Court of Appeals
for the
District of Columbia Circuit

REPLY
BRIEF

IN THE
UNITED STATES COURT OF APPEALS
FOR THE DISTRICT OF COLUMBIA CIRCUIT

United States Court of Appeals
For The District of Columbia Circuit

Nos. 84-1252, 84-1392, 85-1014 ⑤

FILED JUN 14 1985

GEORGE A. FISHER
CLERK

ASSOCIATION OF ETHYLENE OXIDE USERS,

Petitioner,

v.

ROBERT A. ROWLAND, Assistant Secretary,
Occupational Safety and Health
Administration, *et al.*,

Respondents.

PUBLIC CITIZEN HEALTH RESEARCH GROUP, *et al.*,

Petitioners,

v.

ROBERT A. ROWLAND, Assistant Secretary,
Occupational Safety and Health
Administration, *et al.*,

Respondents.

On Petitions for Review of the Secretary
of Labor's Final Standard Concerning
Occupational Exposure to Ethylene Oxide

REPLY BRIEF OF PETITIONER ASSOCIATION OF ETHYLENE OXIDE USERS

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SUMMARY OF ARGUMENT

I. INTRODUCTION

In promulgating its final standard for occupational exposure to ethylene oxide ("EtO"),[1] the Occupational Safety

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[1] 49 Fed. Reg. 25764 (June 22,1984)(to be codified 29 C.F.R. § 1910.1047).

Safety and Health Administration ("OSHA" or the "Agency") refused to consider evidence that a safe threshold level exists for EtO exposure, and determined, based upon a fictional worker exposure profile, that a significant cancer risk persists at exposures _below_ the apparent threshold level. In thus finding a significant risk where none exists, the Agency relied upon insubstantial scientific evidence and employed assumptions or burdens of proof that the Supreme Court rejected in _Industrial Union Department, AFL-CIO_ v. _American Petroleum Institute_, 448 U.S. 607 (1980).

For example, OSHA disregarded pharmacokinetic evidence showing that because of its half-life, EtO is cleared from the body within approximately three hours of exposure, and, therefore, that the vast majority of exposed workers apparently receive a "no-effect" or threshold dose. _See_ Brief of Petitioner Association of Ethylene Oxide Users ("Association Brief") at 9-19, 43-53. Furthermore, in finding a cancer risk for humans at a level (1 ppm) far below that (14 ppm) which the Agency earlier had determined to be consistent with the human cancer data, OSHA relied primarily on a continuous-high-exposure rat study which itself _supports_ a finding of a no-effect dose despite its doubtful value in predicting a risk for occupationally-exposed humans. _See id_. at 15-23.

Similarly, although OSHA concedes that there is _no_ known correlation between mutagenic and cytogenetic effects and _any_ adverse health effects (OSHA Brief at 27-28), OSHA assumed that such effects support the Agency's findings that EtO is a human carcinogen. See id. at 28-30. And finally, OSHA found a (concededly unquantifiable) risk of reproductive hazards for humans based primarily upon a study that involved no contemporaneous exposure-level data ("measurements" were taken years after the claimed exposures) and whose author conceded that his study could not be used to correlate "spontaneous abortions to known levels of ethylene oxide." See id. at 30-33. In light of such evidence, as well as the Agency's assumptions which impermissibly shifted to employers the burden of establishing a safe level of exposure, it is apparent that the Agency acted arbitrarily and capriciously and that the major provisions of the final EtO rule are unsupported by substantial evidence.[2/]

Furthermore, and contrary to the contentions of Petitioners Public Citizen Health Research Group, et al. ("Public Citizen"), the proposed short term exposure limit ("STEL") was equally unsupported by the rulemaking record, and the observations of the Office of Management and Budget ("OMB") to the effect that "the emperor was wearing no clothes" with regard to that issue simply forced OSHA to confront the paucity of its evidence. In fact, the majority of objective scientific "peer reviewers," whose opinions OSHA subsequently solicited, made it clear that the need for a STEL has not been established, simply confirming what OMB and numerous rulemaking

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[2/] Given the page limitation for a reply brief, a point-by-point response to the Brief of Secretary of Labor ("OSHA Brief") is not feasible here. To facilitate the Court's review of the issues addressed by the Association and OSHA, a chart comparing (and indicating the location of) those parties' analyses of the issues and evidence is appended hereto as an addendum.

participants had asserted all along. See Association Brief at 35-40, 58-60.[3]

Given the vital role of EtO sterilizing in protecting life, health, and safety, the importance of carefully scrutinizing OSHA's conduct in this rulemaking cannot be overemphasized. Because many employers, fearing that they will be unable to comply with OSHA's final rule, are likely to abandon EtO sterilization, the deaths and serious illnesses resultant therefrom predictably would far outnumber those which OSHA claims will be prevented by its EtO standard.

For example, in early August of 1984, after the University of Maryland Hospital's neonatal intensive care unit abandoned EtO sterilization "because it anticipated that new OSHA standards would make its use of ethylene oxide unacceptable," an outbreak of Pseudomonas aeruginosa occurred. "In all, seven babies became sick, three of them dying. Six others carried the bacterium but did not become ill . . . . Since the outbreak, the hospital has returned to the gas method of sterilizing the respirators." Baltimore Sun, Aug. 29, 1984, at 3D, col. 5-6. In contrast to this high incidence of death and disease occurring in one location after cessation of EtO use, OSHA estimates that between one and two tenths of a percent of an estimated 71,196 individuals who are or will be "exposed to EtO 8 hours per day, 5 days per week, 46 weeks per year, for 45 years" will contract cancer as a result of such exposure.[4/]

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[3] In light of the lack of evidentiary support in the rulemaking record, as well as the peer reviewers' opposition to a STEL, it would be inappropriate to require OSHA to implement a STEL because of what Public Citizen claims was an "improper involvement" by the Office of Management and Budget. In fact, OSHA's eleventh-hour submission of the "final standard" to OMB on June 14, 1984 suggests that OSHA was itself acting in bad faith and was attempting to buffalo OMB into quickly signing off on the entire large and complex regulation rather than risk placing OSHA in noncompliance with the court order that required the regulation to be published on the following day.

Although it appears that OSHA's EtO rule may well result in more significant adverse health consequences than positive protections, OSHA has failed to respond adequately (if at all) to the demonstrated inadequacies and improprieties in its EtO rulemaking. Accordingly, this Court should find that the Agency has acted arbitrarily and capriciously and has not established that the 1 ppm permissible exposure limit ("PEL") and the required signs and labels are necessary to eliminate a significant risk of harm.[5/]

[4/] See 49 Fed. Reg. at 25768. As more fully set forth below (at 6-16) and in the Association's previously-filed Brief (at 11-22, 33-35, 43-53), OSHA's estimation of the excess cancer risk at 1 ppm necessarily is inaccurate because it is based upon: (1) a concededly overstated worker exposure profile; (2) an assumption that no safe level of exposure can exist; (3) an animal (rat) study of negligible predictive value for humans which itself contains evidence of a safe exposure level; and (4) a failure to take into account the implications of pharmacokinetic factors such as breathing rate differences between rats and humans.

[5/] The Association in this review proceeding does not, as OSHA suggests (OSHA Brief at 55), seek to have this Court "reweigh the evidence" in the rulemaking record. Instead, the

(footnote continued)

II. OSHA IMPROPERLY SHIFTED THE BURDEN OF PROOF IN FINDING A SIGNIFICANT RISK, AND THAT FINDING IS NOT SUPPORTED BY SUBSTANTIAL EVIDENCE

OSHA may not set standards except to eliminate significant risks of harm. Industrial Union Department, AFL-CIO v. American Petroleum Institute, 448 U.S. 607, 639-40, 51 (1980). And OSHA's finding of significant risk must be supported by substantial evidence in the record as a whole if the standard is to be upheld. 29 U.S.C. § 655(f); Industrial Union Department, AFL-CIO v. Hodgson, 499 F.2d 467 (D.C.Cir. 1974).

The core of OSHA's final EtO standard is its conclusion that a "significant risk [of cancer] persisted" at an

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(footnote 5 cont'd)

Association asks the Court to scrutinize the record to determine whether, in substance as well as in form, OSHA considered all relevant matters submitted to it, and whether the Agency described, and articulated the rationale for resolving, significant isssues involved in the EtO rulemaking. See 29 C.F.R. § 1911.18(a) and (b)(1984); American Federation of Labor v. Marshall, 617 F.2d 636, 649-50 (D.C. Cir. 1979); Industrial Union Department, AFL-CIO v. Hodgson, 499 F.2d 467, 475-76 (D.C. Cir. 1974); Association Brief at 45-46. If the Court finds that, as to certain issues crucial to the determination of risk and its significance, the Agency proceeded with an inalterably closed mind, failed to consider an important aspect of the asserted risks of EtO exposure, or left vital questions raised in the rulemaking proceedings unanswered, then the Court must find that OSHA proceeded arbitrarily and capriciously in promulgating its final rule and that the rule must be invalidated. See Association Brief at 47 and cases cited therein. Furthermore, to the extent that the claimed "substantiality" of the evidence supporting OSHA's final rule rests upon the Agency's refusal to consider (adequately, if at all) evidence contradicting the assumptions and data supporting the Agency's significant risk finding, the substantiality and credibility of that evidence is greatly diminished.

level of 1 ppm, the lowest level feasible of control, and therefore, that the PEL should be set at that level. See OSHA Brief at 60, 43-44. And the "quantitative risk assessment" upon which OSHA relied in setting the PEL at 1 ppm was based almost entirely upon a two-year high-exposure rat inhalation study,[6/] the results of which were extrapolated via a mathematical model to infer the cancer risks for humans at specific theoretical exposure profiles which OSHA concedes are unrealistic.[7/]

A. The Legal and Factual Significance of a Safe Threshold Level of Exposure.

The issue of a safe threshold level of exposure to EtO is of crucial legal and factual significance. Thus, if a threshold level exists (i.e., a level at which no "material health impairment" could occur), OSHA could not lawfully set a PEL at or below that level. Industrial Union Department, AFL-CIO v. American Petroleum Institute, 448 U.S. at 639-40, 651. Furthermore, from a factual or evidentiary

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[6/] While other animal and epidemiological (human) evidence in the record was viewed by OSHA as weak but "supportive" (OSHA's brief at 26), it is undisputed that the Bushy Run rat study and the mathematical projections of its results are the real basis for OSHA's justification of a 1 ppm PEL. See OSHA Brief at 62.

[7/] Thus, although OSHA initially took the position that the mathematical model to be utilized in the risk assessment should "permit[] projection of risk levels for human beings at typical exposure levels" (OSHA Brief at 41, citing 49 Fed. Reg. at 25757-63), the Agency now agrees with the Association that few workers will experience the type of exposure profile upon which the risk assessment is based. OSHA Brief at 65. Accordingly, that exposure profile does not provide the basis for a realistic assessment of the actual risks of ETO exposure.

perspective, the existence of a safe level of exposure must be taken into account in the assessment of risk over a range of possible exposure levels if the risk assessment is to have any validity at all. A risk assessment which assigns a theoretical risk where evidence shows that none exists cannot be deemed reliable or valid for standard-setting purposes.[8/]

In the rulemaking record before us, there is undisputed evidence that the body's "clearing mechanisms" remove foreign substances as quickly as possible and render a "no-effect" or "threshold" dose likely for EtO (see Association Brief at 13-15). Furthermore, even the rats in the Bushy Run study (upon which OSHA's risk assessment was based) showed statistically significant increases in mortality and cancer rates only at exposure levels of 33 ppm or above, and there were no statistically significant differences between the control group rats and rats exposed to 10 ppm. See 49 Fed. Reg. at 25740-42.[9/]

[8/] OSHA's Cancer Policy, of course, precludes any "determination . . . that 'threshold' or 'no-effect' levels of exposure can be established," 29 C.F.R. § 1990.143(h), and OSHA concedes that its analysis in the EtO rulemaking "is consistent with the approach to analysis of evidence set forth in the Cancer Policy." OSHA Brief at 58. In fact, OSHA has affirmed that one of the "primary assumptions" used in its quantitative risk assessment was that "there is no 'threshold' level below which EtO exposure is harmless." OSHA Brief at 42, n.38.

[9/] As discussed below, at pp. 13-14, breathing rate and other species differences between rats and man result in rats taking

(footnote continued)

Finally, in light of OSHA's concession that the epidemiological evidence (which the Agency now claims is "supportive" of the significant risk finding) "contained no direct evidence of an excess risk of cancer at chronic exposure levels below approximately 14 ppm,"[10] the rulemaking record (_including_ the Bushy Run study) clearly would _support_ a finding that a safe threshold level for EtO exposure may be established, and the existence of a threshhold level necessarily was an issue of great significance in this rulemaking.

OSHA did not, however, raise this issue in any meaningful way,[11] and the Agency "never even asked for comments on whether there was a safe level of exposure. . . ." _United Steelworkers of America AFL-CIO-CLC_ v. _Marshall_, 647 F.2d 1189, 1247 (D.C. Cir. 1980), _citing_ _Industrial Union Department_ v. _American Petroleum Institute_, 448 U.S. at 623. And contrary to

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(footnote 9 cont'd)

up an equivalent dose four to seven times greater than that taken up by a human at the same exposure level, and OSHA neither considered and resolved that issue during rulemaking nor rebutted the Association's description of the effects of these species differences.

[10] Memorandum of Points and Authorities in Support of Defendant's Motion for Summary Judgment ("OSHA's Summary Judgment Memorandum") at 19, _Public Citizen Health Research Group_ v. _Auchter_, 554 F. Supp. 242 (D.D.C. 1983).

[11] Thus, in the entire 34-page notice of proposed rule, OSHA's only allusion to this issue was its statement that "[t]here is no threshold effect assumed" in performing the quantitive risk assessment. 48 Fed. Reg. 17284, at 17293 (April 21, 1983).

the Agency's claims (OSHA Brief at 59), it did not "specifically consider[] and reject[] the evidence the Association claims should be considered dispositive of this issue."

B. By Presuming That There is no Threshold Level, OSHA Improperly Shifted The Burden of Proof

Not only has the Supreme Court made it clear that OSHA bears the burden of proof to show by substantial evidence that its standard is necessary to prevent a significant risk of material health impairment, Industrial Union Department v. American Petroleum Institute, 448 U.S. at 653-54, the Court insisted that the Agency may not shift to employers the burden of "proving that a safe level of exposure exists." Id. at 635, n.39. By "assuming" that there can be no safe level of exposure to EtO, by not seeking evidence on the issue, and by disregarding such evidence when it assessed the risk of exposure, OSHA has employed a burden-shifting presumption that no safe exposure level exists.

A presumption generally has the effect of placing upon the opposing party the burden of establishing the nonexistence of the presumed fact, once the party invoking the presumption establishes the basic fact giving rise to it. See McCormick's Handbook of the Law of Evidence, 826 (2d ed. 1972); Fed. R. Evid. 301 advisory committee note. In fact, inasmuch as OSHA totally ignored evidence concerning the existence of threshold levels (including its own prior view that there is no evidence of an excess cancer risk at exposure levels below 14 ppm), OSHA treated its presumption as conclusive or irrebuttable. Accordingly, not only has OSHA shifted to employers the burden of proving that a safe level of exposure exists for EtO, OSHA's conclusive presumption rendered that burden an "impossible" one because the Agency disregarded record evidence supporting the establishment of a threshold level. See Industrial Union Department v. American Petroleum Institute, 448 U.S. at 635, n.39.

OSHA has not adequately rebutted or responded to the Association's demonstration that the Agency proceeded improperly in this rulemaking. First, OSHA's attempt to justify its primary reliance on the Bushy Run study as a basis for risk assessment clearly does not succeed. Contrary to OSHA's assertion (OSHA Brief at 61, n.47), the Agency apparently has "revised its opinion" of the utility of human cancer risk assessment based upon the Bushy Run study. Thus, OSHA earlier had enumerated the limitations on the reliability of a quantitative risk assessment projected from the Bushy Run data:

> [G]uidelines for projections of the data were not a matter of scientific consensus; the numbers generated might reflect very high estimates; and the proper scaling factors for conversion from animal to human dose predictions were not definitely known . . . . Additionally, the quantitative risk assessment addressed lifetime risk from 45-year chronic occupational exposure, . . . while the exposures documented to the Agency were intermittent or at very low levels.

OSHA's Summary Judgment Memorandum at 9, n.14.

OSHA's concessions that actual worker exposures to EtO are "intermittent or at very low levels" (id.) and that "few workers will have an 8 hour/day, 5 day/week, 45 year working lifetime exposure to EtO" (OSHA Brief at 65) simply highlights the inherent circularity of the Agency's reasoning in estimating a purportedly "real" ("significant") risk for exposed workers based upon a _fictional_ (and inflated) exposure profile. The Act's requirement [29 U.S.C. § 655(b)(5)] that a toxic substance standard protect chronically-exposed employees over their working lifetimes does _not_ require that OSHA over-estimate the actual risk of such exposure as a means of affording that protection. Accordingly, contrary to OSHA's contention (OSHA Brief at 65-66), the Act does not support the Agency's reliance upon an inflated worker exposure profile in estimating the significance of risk.

Furthermore, in view of the Agency's above-described concessions concerning the limitations of a risk assessment based on the Bushy Run study, it is all the more surprising that OSHA considers that the viral infection of the subject rats and their tendency to spontaneously develop tumors should not be deemed to affect the reliability of the Bushy Run study as a data base.[12/] _See_ OSHA Brief at 61-63.

[12/] In fact, when rats exposed to 50 ppm EtO in a study conducted by the National Institute for Occupational Safety and Health ("NIOSH"), the health research arm of OSHA (_see_ 29 U.S.C. §671), showed a greater incidence of leukemia than those exposed to 100 ppm, NIOSH explained that "these preliminary results must be interpreted in light of the known spontaneous incidence of leukemia in Fischer 344 rats." 49 Fed. Reg. at 25742. _See also_ Association Brief at 21, n.17. Furthermore, because the Association does not contend that a viral infection would convert a non-carcinogen into a carcinogen (_see_ OSHA Brief at 23-24), the testimony of Dr. J.M. Ward (quoted by OSHA) that it would not do so is irrelevant and begs the more important question of whether such an infection might facilitate a chemical's carcinogenicity or might increase the rate of spontaneously developing cancers.

Second, contrary to OSHA's claim that it considered differences in breathing rates between rats and humans and related pharmacokinetic issues (OSHA Brief at 63-64, citing 49 Fed. Reg. at 25760),[13] nothing on the cited page of the final rule's Preamble supports OSHA's contention that its "resolution of this issue [i.e., the effect of breathing rate differences and other pharmacokinetic considerations] is . . . supported [by] substantial evidence on the record." OSHA Brief at 64. In fact the standard breathing rate adopted (49 Fed. Reg. at 25760) was just that, a breathing rate, not (as OSHA contends) a "conversion rate" for equivalent doses between rats and man. Furthermore, although OSHA admitted earlier in the Preamble that "the effects of possible differences in dosage, dynamics of exposure, metabolism, pharmacokinetics and repair mechanisms between species [i.e., between rats and humans] . . . may increase uncertainty in the final risk estimates . . . ," instead of evaluating and "resolving" these issues, OSHA simply brushed them aside by observing that they "are not specific to ethylene oxide" and that "OSHA [has] concluded with confidence that EtO should be considered a potential human carcinogen." 49 Fed. Reg. at 25756. Accordingly, OSHA's "resolution" of this issue was based not on substantial evidence but on an evasion of the uncertainties which consideration of pharmacokinetic issues introduces into the risk assessment.

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[13] As fully set forth in the Association Brief at 15-18, these species differences result in rats taking up a relative dose per body weight of from four to seven times that absorbed by humans at equivalent exposure levels. Thus, the 33 ppm continuous exposure level at which the Bushy Run rats showed statistically significant increased cancers would translate to a human exposure level in the range of 132-254 ppm, whereas the 10 ppm exposure level at which no significantly increased cancers appeared would translate to a human exposure level in the range of 40-70 ppm. Accordingly, although the Bushy Run study may not provide a reliable basis for predicting human cancer risk, it clearly supports a finding that a threshold or safe EtO exposure level may be determined.

Third, OSHA has totally omitted to respond to the Association's description of the computational errors of Dr. K. Crump (OSHA's mathematical modeling expert) and of Dr. Crump's concession that he did _not_ consider pharmacokinetic issues in the mathematical model he used to extrapolate human cancer risk from the Bushy Run rat data. _See_ Association Brief at 15-18. In fact, Crump's and OSHA's computations were based upon an _assumption_ that "breathing rate is proportional to [lung] surface area (which in turn is proportional to body weight. . .)," an assumption which does not account for metabolism or the _rate_ at which the lungs function, and which suggests, contrary to the undisputed findings of Darby and EPA, that humans have a "breathing rate" approximately 38 times that of rats. _Compare_ Testimony of K. Crump (Ex. 34) at 13-14, _with_ Association Brief at 15-18.

In summary, OSHA's refusal to address the issue of threshold levels and its failure to consider the effects of species differences in breathing rates, metabolism, clearing, repair mechanisms, and other pharmacokinetic issues were arbitrary and capricious and render invalid its projection of human risk based upon the Bushy Run rat inhalation study.

III. THE EPIDEMIOLOGICAL DATA OSHA DEEMS "SUPPORTIVE" OF ITS SIGNIFICANT RISK FINDING PROVIDE NO ADEQUATE BASIS FOR PREDICTING ADVERSE HEALTH EFFECTS

A. OSHA's Reliance on the Concededly Weak and Inconclusive Epidemiological Studies is Misplaced.

Despite OSHA's concessions that the epidemiological cancer data (including the Morgan and Hogstedt studies) are weak and inconclusive (OSHA Brief at 26) and that there is no known correlation between mutagenic and cytogenetic effects and _any_ adverse human health effects (OSHA Brief at 27, 28, n.19), OSHA contends that these epidemiological data are "supportive" of its significant risk findings, and, accordingly, describes these studies at great length. OSHA Brief at 18-22; 31-35.

Although the Association already has documented the considerable problems and weaknesses of these studies [Association Brief at 23-33; Petition of Association of Ethylene Oxide Users for Stay of Effective Date and for Reconsideration of Final Ethylene Oxide Rule ("Association's Petition") at 14-21], it bears reemphasizing that OSHA earlier had concluded that the epidemiological evidence contains "no direct evidence of an excess risk of cancer at chronic exposure levels below approximately 14 ppm TWA" (OSHA's Summary Judgment Memorandum at 19), and that the Environmental Protection Agency ("EPA") refused to rely upon human cancer data (including the Hogstedt studies) because they are "too uncertain to do anything with." _See_ Association Brief at 19, _citing_ EPA's Health Assessment

Document for Ethylene Oxide at 9-139.[14]

The Johnson & Johnson study (Ex. 4-17 at 2, 9, Figure 1) showed statistically higher sister chromatid exchange ("SCE") rates for employees in Plant III (exposed at levels estimated to be 5-200 ppm). "A much less pronounced trend was observed at Plant II (estimated exposures of 1-10 ppm) and then only on initial testing. Id. at 9. Significantly, the Plant II controls had higher SCE's than low-exposed employees on initial testing, and six months later, Plant II employees showed no significantly increased SCE's. Id. at Figure 1. OSHA also has omitted to explain (OSHA Brief at 33, n.28) that the reason that the Johnson & Johnson study employed two sets of controls (the second being non-employees), was, as Johnson & Johnson explained, "the SCE levels in the control group of presumably unexposed employees at Plant III were higher than the results for the other control groups," and that this unforeseen result "led to a modification . . . of the study design." Ex. 4-17, at 5. This post-study modification nullifies the results of the Johnson & Johnson study and OSHA's reliance thereon.

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[14] And as Dr. K. Crump stated in his testimony, "Morgan et al. found fewer deaths from malignancies than expected . . . ; no leukemias were found, whereas 0.7 were expected." Ex. 34 at 4. A similar uncertainty attaches to the 1981 Pero study (Ex. 6-12, OSHA Brief at 31-32) because, in addition to the potential confounding effects of methyl formate and other problems (see Association's Petition for Stay at 19-21), the study claims exposure levels at a range (0.5 to 1 ppm) that is below the accuracy range of any then-available monitoring technology. See Association Brief at 37-40.

While OSHA may rely upon the "cumulative effect" of even the "inconclusive but suggestive results of numerous studies" _if_ that cumulative effect "presents a rational basis" for standard setting,[15] it is difficult to comprehend how OSHA can characterize the weak epidemiological evidence in this record as supporting its finding that a significant risk of cancer persists at 1 ppm exposure levels in view of its own evaluation of that same evidence as showing _no_ excess cancer risk at exposure levels below 14 ppm and in view of EPA's rejection of the epidemiological cancer data as providing any basis for risk assessment.

B. In View of Record Evidence Demonstrating a Safe Threshold Level of Exposures vis-a-vis Reproductive Effects, OSHA's Reliance Upon the Hemminki Study is Inappropriate.

Despite the many demonstrated problems with the Hemminki study (_see_ Association Brief at 30-33), including Dr. Hemminki's concessions that he took _no_ contemporaneous measurements of EtO levels and that "our series is not large enough to compare abortion rates and known ethylene oxide concentrations" [286 Brit. Med. J. 1976, 1977 (June 18, 1983)], OSHA has relied primarily upon the Hemminki study in concluding that there is "sufficient qualitative evidence in the rulemaking record to indicate that EtO poses a reproductive hazard for both men and women." 49 Fed. Reg. at 25752.[16]

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[15] _United Steelworkers of America_ v. _Marshall_, 647 F.2d 1189, 1253 (D.C. Cir. 1980) (citations omitted).

[16] OSHA claimed that a fetotoxic hazard, suggested by the Hemminki report, was supported by the studies of Hackett, (footnote continued)

At the outset, it must be emphasized that OSHA found only a "qualitative" risk of reproductive hazard from EtO exposure. In other words, EtO exposure poses some risk of such a hazard. However, the Agency found no data which would support a quantitative risk assessment that would permit the Agency to determine the significance of such a risk, if any, at specific levels of occupational exposure to ethylene oxide. See OSHA Brief at 39.

In fact, the record contains substantial evidence that, as in the case of carcinogenicity, there is a safe threshold level for EtO exposure vis-a-vis reproductive hazards. Thus, in a study of rats exposed at 10, 33, and 100 ppm conducted at the Bushy Run Research Center (Exs. 2-33, 54), only the rats exposed at 100 ppm showed significantly fewer offspring per litter, and a dose-response relationship between fertility and EtO exposure was observed at 33 and 100 ppm. "However, no statistically significant adverse effects following exposure to 33 ppm or 100 ppm were detected." OSHA Summary Judgment Memorandum at 12-13, emphasis supplied. Accordingly, if the evidence on reproductive hazards is "supportive" of anything, it clearly

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(footnote 16 contin.)

Jones-Price, and LaBorde and Kimmel. 49 Fed. Reg. at 25754. These animal studies, however, involved either chronic inhalation of extremely high levels of EtO or intravenous injection of the substance, neither of which reflects human exposures. Thus, the Hackett study involved rats exposed to 150 ppm of EtO for 7 hours per day, 5 days per week, while the latter two studies involved intravenous injection of EtO into rabbits (Jones-Price) and mice (LaBorde and Kimmel). Id. at 25748. Similarly, all other studies OSHA mentioned as supporting an "indication" that EtO is a "potential reproductive hazard" involved animals rather than humans. See 49 Fed. Reg. at 25749, and Ex. 47 at 49.

supports both a finding that a threshold level exists and the incorporation of a threshold level into any quantitative assessment of the significance of the risks of EtO exposure.

IV. OSHA's COMPARISON OF INDUSTRIAL FATALITY STATISTICS WITH THE MATHEMATICALLY-PROJECTED HYPOTHETICAL "BENEFITS" OF THE ETO STANDARD IS RENDERED MEANINGLESS BY OSHA'S FAILURE TO ACCOUNT FOR THRESHOLD LEVELS AND ITS UNREALISTIC EXPOSURE PROFILES.

As previously demonstrated (*supra* at 7-13; Association Brief at 13-22, 33-35), OSHA's refusal to account for the existence of threshold exposure levels and species differences in breathing rates, relative dose uptake, metabolism, repair mechanisms, and other pharmacokinetic issues, as well as its assumption of concededly unrealistic worker exposure profiles necessarily resulted in an overinflated assessment of the significance of risk. In an additional attempt to bootstrap the credibility of its final EtO standard, the Agency has compared "EtO cancer risk with accident fatality rates based upon figures . . . compiled by the Bureau of Labor Statistics." OSHA Brief at 45-46, n.41. *See also* 49 Fed. Reg. at 25764. Thus, comparing its "estimate of excess cancer risk at 50 ppm EtO" (between 634 and 1093 per 10,000 exposed employees) with the lifetime fatality risks in manufacturing (27 per 10,000) and service employment (16 per 10,000), OSHA concludes that the "cancer risks associated with EtO . . . at 50 ppm are higher than accident fatality risks from all types of accidents combined, in most industries." 49 Fed. Reg. at 25764.

This comparision of the concededly limited and hypothetical assessment of EtO cancer risk with industrial fatality risks based upon actual occupational accident statistics not only is specious in itself, it highlights the fact that OSHA's quantitative risk assessment has little or nothing to do with the real effects of EtO exposure. If OSHA's EtO risk assessment projections were accurate, almost 1 out of every 10 exposed employees would have incurred a cancer-related death at exposures at the previous PEL of 50 ppm, and it is inconceivable that health professionals would not have detected such a cancer epidemic.

Since EtO has been used as a sterilant and pesticide for over 40 years, often at much higher concentrations than those currently in use, an epidemic such as that predicted by OSHA's risk assessment surely would have surfaced by now. Contrary to OSHA's claim that "the long latency period for the appearance of cancers (20 to 40 years in some instances)" justified its reliance on the Bushy Run study data projections (OSHA Brief at 64-65), Dr. Crump observed that there is only a three to four year latency period for environmentally induced leukemia in humans. Ex. 34 at 22.

Finally, as discussed above (at pp. 4-5), the likelihood of death and serious illness resultant from even sporadic abandonment of EtO sterilization predictably will be far greater than either OSHA's projected risks from EtO exposure at the old PEL of 50 ppm or the typical fatality risks in the manufacturing industry. Against this background, it is apparent that OSHA's attempt to justify its necessarily overinflated risk assessment by comparison to industry fatality risks discredits the risk assessment itself.

V. OSHA'S SIGNS AND LABELS REQUIREMENT IS NOT SUPPORTED BY THE RULEMAKING RECORD

As a part of "[a]ny standard promulgated" under Section 6(b) of the Act [29 U.S.C. § 655(b)], OSHA is required to "prescribe the use of labels or other appropriate forms of warning as are necessary to insure that employees are apprised of all hazards to which they are exposed. . . ." Section 6(b)(7), 29 U.S.C. § 655(b)(7). This requirement, of course, applies to the EtO standard which was promulgated under Section 6(b)(5) of the Act [29 U.S.C. § 655(b)(5)]. However, because the final EtO standard's requirement of signs and labels stating that EtO is a "CANCER AND REPRODUCTIVE HAZARD" is not based upon a finding (or upon evidence showing) that such signs and labels are necessary to reduce or eliminate a significiant risk of harm that requirement is invalid. See Association Brief at 55-58.

OSHA contends that the Supreme Court in Industrial Union Department set forth a "legal test applicable to individual provisions of" the ethylene oxide standard, i.e., that while Secretary must show the "standard as a whole addresses and substantially reduces a significant risk . . ., the signs and labels requirement . . . need not in itself significantly reduce the risk of employee harm . . ., but instead must contribute in a reasonable way to the standard's -- and the Act's -- overall purpose of protecting employees from significant risks of harm." OSHA Brief at 69. OSHA further contends that the Association "misreads" this legal test when it argues that nothing in the administrative record suggests that signs and labels stating that EtO is a "CANCER HAZARD AND REPRODUCTIVE HAZARD" are necessary to eliminate a significant risk of harm. *Id*.

Contrary to OSHA's contentions, however, neither the Supreme Court (at the cited pages or elsewhere) nor the other cases cited by OSHA[17/] describe the alleged "test." Rather, as the Court stated in *Industrial Union Department*, "before he can promulgate *any* permanent health or safety standard [the Secretary] is required to make a threshold finding that . . . *significant risks are present and can be eliminated or lessened by a change in practices*." 448 U.S. at 642, emphasis supplied. Similarly, "the Act . . . requires the Agency to *limit* its endeavors in the standard-setting area to eliminating significant risks of harm." *Id.* at 651, emphasis supplied. And finally, the Court emphasized that in order for OSHA to justify a *particular* requirement of the benzene standard (*i.e.*, a ban on dermal contact), "the agency must find such a ban is 'reasonably necessary and appropriate' to remove a significant risk of harm from such contact." *Id.* at 662.

Neither this Court's *United Steelworkers* decision nor the Supreme Court's holding in *Mourning* states or implies a different test for the validity of individual provisions of occupational safety and health standards promulgated under the authority of 29 U.S.C. § 655(b). Thus, in *Mourning* (a case having nothing to do with the Occupational Safety and Health

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[17/] *United Steelworkers of America*, 647 F.2d at 1237, *citing Mourning v. Family Publications Service, Inc.*, 411 U.S. 356, 369 (1973).

Act), the Supreme Court addressed the test to be applied in determining whether an agency has exceeded its rulemaking authority "[w]here the empowering provision of [the] statute states simply that the agency may 'make . . . such rules and regulations as may be necessary to carry out the provisions of this Act." 411 U.S. at 369-40. The Court held that a regulation promulgated under such a broad empowering provision "will be sustained so long as it is reasonably related to the purposes of the enabling legislation." Id., citations omitted. Similarly, in upholding OSHA's earnings protections program for medically-removed workers in the United Steelworkers case, this Court did not hold or suggest that a broader test than that announced by the Supreme Court in Industrial Union Department should be applied to individual requirements of a standard promulgated under 29 U.S.C. § 655(b). See 647 F.2d at 1236-38.

Clearly, requiring employers to employ the specified signs and labels is a "change in practices" which OSHA has failed to demonstrate is "reasonably necessary and appropriate" to remove a significant risk of harm, and the Agency's proposed "legal test" concedes as much. Accordingly, and in view of the lack of substantial evidence showing that EtO is a cancer or reproductive hazard at occupational exposure levels below 10 ppm, the Association submits that the signs and labels requirement is indeed unsupported by the rulemaking record, and should be invalidated and remanded with a direction that the Agency require only signs and labels which are so supported (e.g., signs and labels which state that EtO is extremely toxic at high levels and long exposures, and which carry appropriate warnings concerning safe use, including a warning not to breathe vapors).

CONCLUSION

Although it is apparent that a safe threshold level may in fact be determinable for EtO exposure, OSHA's failure to account for threshold levels in its assessment of the risk, as well as its disregard of pharmacokinetic issues and its unrealistic assumptions concerning worker exposure profiles, necessarily resulted in a substantially inflated finding of the significance of the risk of cancer from EtO exposure. Accordingly, because the Agency has acted arbitrarily and capriciously in making its significant risk finding and has relied upon insubstantial evidence, the 1 ppm PEL and the signs and labels requirement of the final EtO rule should be invalidated and remanded to the Agency with directions that it take safe threshold levels into account in setting a PEL for EtO exposure and that it demonstrate with substantial evidence in the record that any signs and labels to be required are necessary to avoid a significant risk of harm.

Respectfully submitted,

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ADDENDUM

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ISSUE/EVIDENCE	OSHA BRIEF	ASSOCIATION BRIEF	COMMENTS/HIGHLIGHTS
I. EtO Carcinogenicity:			
A. Epidemiological Studies	18-22	23-27	*OSHA concedes that the "epidemiological evidence" contains "no direct evidence of an excess cancer risk at levels below 14 ppm." OSHA Brief at 61, n.47. Also such evidence has "weaknesses" and is "not conclusive" but is deemed "suggestive." Id. at 26.
1. Hogstedt I	19, 21	23-27	
2. Hogstedt II	19-21	23-27	
3. Morgan	20-21	25	*OSHA has conceded that workers in Hogstedt studies "were exposed to other suspect carcinogenic substances," sometimes "at very high levels." See Association Brief at 24, quoting OSHA's Summary Judgment Memorandum at 10, n.15.
B. Experimental Evidence	22-26	19-22	*In contrast to human exposures (which are typically low-level and intermittent), the subject animals in these studies were exposed continuously at extremely high levels. See Association Brief at 19.
1. Bushy Run Rat Study	22-24, 62-63	19-22; see also Memorandum of Petitioner of Association of Ethylene Oxide Users in Support of Motion for Stay Pending Review, No. 84-1252, at 12-15	*There is no scientific basis for assuming that effects of exposure are the same at high and low levels, id., and OSHA in fact concedes that "the effects of EtO are presumed to be dose dependent." Id. at 18 quoting 50 Fed. Reg. at 73. See also Association Brief at 15-18, OSHA Brief at 25-26.

ISSUE/EVIDENCE	OSHA BRIEF	ASSOCIATION BRIEF	COMMENTS/HIGHLIGHTS
2. NIOSH (Rats/ Monkeys)	24-25	Memorandum in Support of Motion for Stay, at 12-15	*Bushy Run found no statistically significant differences in rats continously exposed to 10 ppm; only in rats exposed at 33 ppm and above. 49 Fed. Reg. at 25740-42. NIOSH rats showed greater incidence of leukemia at 50 ppm than at 100 ppm. Id. at 25742. Bushy Run monkeys showed no increased leukemia. Id. at 25742-43.
C. Mutagenic/ Ctyogenetic Effects	27-35; 66-68	28-30; 54	*OSHA concedes that there is no known correlation between mutagenic and cytogenetic effects and any adverse health effects. OSHA Brief at 27, 28, n.19. *All animals in studies cited by OSHA were exposed to EtO in a manner (injection) or at extremely high levels not experienced by humans. Thus, Embree involved "inhalation of extremely high concentrations" (OSHA Brief at 28), as did Cumming (OSHA Brief at 29), NIOSH (id. at 29-30, n.24) and Yager/Benz (id. at 30-31, n.25). Generoso involved injection (id. at 29). *Dr. Yager concedes that sister chromatid exchanges can result from a variety of causes other than EtO, including smoking, drugs and stress. Association Brief at 29. *OSHA concedes that the evidence concerning mutagenic/cytogenetic effects provides no basis for quantification of risk. OSHA Brief at 39.
1. Experimental Evidence	28-31		
2. Epidemiological Evidence	31-35	28-30	
a. Pero	31-32	28; see also Association's Reply Brief at 15, n.14	
b. Johnson & Johnson	32-33	28; see also Association's Reply Brief at 16	
c. Yager	34-35	28-30	

ISSUE/EVIDENCE	OSHA BRIEF	ASSOCIATION BRIEF	COMMENTS/HIGHLIGHTS
II. Reproductive Effects			
A. Experimental Evidence	35-36, 39	30-31, n.24	*OSHA concedes that evidence concerning reproductive effects provides no basis for quantification of risk (i.e. assessment of significance of risk). OSHA Brief at 39.
B. Hemminki Study	36-38	30-33	*Dr. Hemminki admits that his study is not based on contemporaneous exposure data and could not serve as basis for comparison of abortion rates at specific levels. See Association Brief at 32.
III. Quantification of Risk	40-47; 61-66	11-22; 33-35; 48-55	*Despite both human and animal evidence that a safe threshold exposure level exists for EtO exposure, OSHA presumed that no such safe level could be determined. See Association Brief at 11-18; 48-53.
A. Reliance on Rat Cancer Data	41-44; 41-64	9-11; 19-22; 44; 52	
B. Presumption of No Threshold Dose	42, n.38; 57-60	11-15; 48-53	
C. Disregard Breathing Rates, Other Species Differences	56-57; 63-64	15-18; 51	*Although the existence of a safe threshold level was of crucial significance in this rulemaking, OSHA did not even seek comments on the existence of a threshold, and disregarded evidence that such a threshold exists. Association Brief at 12-18.
D. Fictional Worker Exposure Profile	65-66	11; 33-35; 52-53	
E. Lowest Feasible PEL Based on Inflated Significance of Risk	44-47; 60-61	11; 49; 53	*OSHA concedes that the worker exposure profile upon which it based its estimation of the significance of cancer risk overstates actual worker exposures. OSHA Brief at 65.

ISSUE/EVIDENCE	OSHA BRIEF	ASSOCIATION BRIEF	COMMENTS/HIGHLIGHTS
IV. Signs and Labels	68-70	55-58	*OSHA's proposed legal test for validity of individual requirements of a health and safety standard concedes that the Agency did not find its signs and labels requirement to be necessary to remove a significant risk of harm, as the Supreme Court required in Industrial Union Department v. American Petroleum Institute, 448 U.S. at 642.